

(19)



Europäisches Patentamt
European Patent Office
Office européen des brevets



(11) Publication number : **0 661 034 A1**

(12)

EUROPEAN PATENT APPLICATION

(21) Application number : **94309772.5**

(51) Int. Cl.⁶ : **A61K 6/00, A61K 6/083**

(22) Date of filing : **23.12.94**

(30) Priority : **28.12.93 JP 336957/93**

(43) Date of publication of application :
05.07.95 Bulletin 95/27

(84) Designated Contracting States :
DE FR GB

(71) Applicant : **TOKUYAMA CORPORATION**
1-1, Mikage-cho
Tokuyama-shi Yamaguchi-ken (JP)

(72) Inventor : **Ohno, Hideki**
c/o Tokuyama Corporation,
1-1, Mikage-cho
Tokuyama-shi, Yamaguchi-ken (JP)

Inventor : **Kimura, Mikio**
c/o Tokuyama Corporation,
1-1, Mikage-cho
Tokuyama-shi, Yamaguchi-ken (JP)
Inventor : **Fuchigami, Satoru**
c/o Tokuyama Corporation,
1-1, Mikage-cho
Tokuyama-shi, Yamaguchi-ken (JP)
Inventor : **Oguri, Makoto**
c/o Tokuyama Corporation,
1-1, Mikage-cho
Tokuyama-shi, Yamaguchi-ken (JP)

(74) Representative : **Cresswell, Thomas Anthony**
J.A. KEMP & CO.
14 South Square
Gray's Inn
London WC1R 5LX (GB)

(54) **Dental composition.**

(57) A dental composition containing an acid such as maleic acid, phosphoric acid or citric acid ; an acid group-containing (meth)acrylate monomer having for example a carboxyl group or a phosphoric acid group ; an organosulfonate and/or an organosulfinate such as a sodium benzenesulfonate or a sodium p-toluenesulfinate ; a water-soluble organic solvent such as ethanol or propanol ; water ; and optionally further comprising a hydroxy- or a dihydroxyalkyl(meth)acrylate monomer. The composition is useful as a pre-treatment agent to improve adhesion of dental filling material to teeth.

EP 0 661 034 A1

DETAILED DESCRIPTION OF THE INVENTION

(Field of the Invention)

5 The present invention relates to a dental composition that is suited for use as a pre-treatment agent for accomplishing a high adhesive strength between a dental filling material and a tooth at the time of filling and repairing the tooth in the field of dental treatment.

(Prior Art)

10 Dental filling materials called composite resins are mainly used for repairing teeth that are damaged by dental caries. Generally, the composite resin is filled in a cavity of a tooth and is then polymerized and cured. However, this material has no adhesiveness to the tooth and, hence, a dental adhesive is used in combination. The adhesive should have adhesive strength that is large enough to overcome the internal stress that gener-
15 ates when the composite resin cures, i.e., large enough to overcome the tensile strength that generates at an interface between the composite resin and the tooth. Otherwise, the composite resin may fall off after used for extended periods of time, or form a gap at the interface between the composite resin and the tooth per-
mitting the infiltration of bacteria that adversely affect dental pulp.

Because the hard tissue of a tooth consists of enamel and dentin, the adhesive should have adhesiveness
20 to both of them. In order to improve adhesiveness, so far, a method has heretofore been employed according to which the surface of a tooth is pre-treated prior to applying the adhesive. As a material for effecting the pre-treatment, an acid-containing aqueous solution is generally used to decalcify the surface of the tooth, such as an aqueous solution containing phosphoric acid, citric acid, maleic acid or the like acid. In the case of the enamel, it is said that the adhesion mechanism to the treated surface is a macroscopic mechanical retention
25 in which the adhesive infiltrates into, and cures in, the coarse surface created by decalcification with an acid-containing aqueous solution. In the case of the dentin, it is said that the adhesion mechanism is a microscopic mechanical retention in which the adhesive infiltrates into, and cures in, fine openings of collagen fiber network exposed on the surface of the tooth after decalcification. However, because the adhesive does not infiltrate
30 into collagen fiber so easily as into the enamel surface, an infiltration promoting agent called primer is usually applied after decalcification. However, this procedure makes the operation cumbersome. In order to simplify the operation, Japanese Laid-Open Patent Publication No. 123515/1985 is disclosing a pre-treatment com-
position comprising an unsaturated carboxylic acid, a (meth)acrylic ester monomer and an organosulfinate. However, even this composition does not realize sufficient adhesive strength to the tooth.

There further arises another problem in that when the enamel and the dentin are simultaneously treated
35 with above-mentioned acid-containing aqueous solution that is generally used, the enamel should be strongly decalcified to obtain a sufficient adhesive strength causing, however, dentin to be subjected to excess decalcification. That is, chips called smear intimately adhere on the surface of the dentin that is ground for the purpose of forming a dental hole and form a smear layer thereon. The smear infiltrates from the surface of the dentin into fine tubes in the dentin communicating to the dental pulp, causing the fine tubes to be clogged
40 with plugs called smear plugs. However, the excess degree of deliming removes the smear plugs so that the permeation through fine tubes in the dentin increases (Shinkai, Kato, Journal of 35(3), 634, 1992) arousing, however, a problem in that harmful substances easily infiltrate into the dental pulp through fine tubes. In recent years the idea that excess decalcification damages dentin that is a vital tissue is becoming widely accepted. Therefore, it is desired to suppress the decalcification of dentin as small as possible.

45 In the art of restoring dental cavity by effecting the pre-treatment, applying an adhesive and filling a composite resin under the above-mentioned circumstances, it has been desired to develop a material that can be used as a pre-treatment material without requiring cumbersome operation of applying a primer, that exhibits high adhesive strength to both the enamel and the dentin, and that decalcifies the dentin to a suitable degree leaving smear plugs.

50 The present inventors have conducted keen study in an effort to overcome the above-mentioned technical assignments and have found the fact that a composition comprising an acid, an acid group-containing (meth)acrylate monomer, an organosulfonate and/or an organosulfinate, a water-soluble organic solvent and the water, can be used as a pre-treatment agent that exhibits a high adhesive strength to the enamel and to dentin without any primer, leaving a suitable degree of smear plugs in dentin.

55 The inventors have further found the fact that a composition comprising an acid, an acid group-containing (meth)acrylate monomer, an organosulfonate and/or an organosulfinate, a water-soluble organic solvent, the water and a hydroxy- or a dihydroxy(meth)acrylate monomer, can be used as a pre-treatment agent that exhibits a high adhesion strength to enamel and to dentin without any primer, leaving a suitable degree of smear

plugs in the dentin.

The present application provides, in a first embodiment, a dental composition comprising (A) an acid having an acid dissociation constant (hereinafter abbreviated as pKa) of not larger than 4, (B) an acid group-containing (meth)acrylate monomer, (C) an organosulfonate and/or an organosulfinate, (D) a water-soluble organic solvent, and (E) the water, wherein a blending amount of (A) is from 5 to 200 mmol with respect to the total amount of 100 g of (B), (C), (D) and (E), and blending amounts of (B), (C), (D) and (E) are from 1 to 30 parts by weight, 1 to 20 parts by weight, 10 to 90 parts by weight, and 5 to 80 parts by weight, respectively, with respect to the total amount of 100 parts by weight of (B), (C), (D) and (E).

In a second embodiment the invention is concerned with a dental composition comprising (A) an acid having an acid dissociation constant (hereinafter abbreviated as pKa) of not larger than 4, (B) an acid group-containing (meth)acrylate monomer, (C) an organosulfonate and/or an organosulfinate, (D) a water-soluble organic solvent, (E) the water, and (F) a hydroxy- or a dihydroxy(meth)acrylate monomer, wherein a blending amount of (A) is from 5 to 200 mmol with respect to the total amount of 100 g of (B), (C), (D), (E) and (F), and blending amounts of (B), (C), (D), (E) and (F) are from 1 to 30 parts by weight, 1 to 20 parts by weight, 10 to 90 parts by weight, 5 to 80 parts by weight, and 1 to 40 parts by weight, respectively, with respect to the total amount of 100 parts by weight of (B), (C), (D), (E) and (F).

There is no particular limitation upon the acid that is used in the present invention provided its pKa is not larger than 4, and any known inorganic acid or organic acid can be used. When pKa exceeds 4, it becomes difficult to decalcify the tooth to a sufficient degree, and practicable adhesive strength is not obtained. The pKa of a polybasic acid is calculated from a dissociation constant in a first stage.

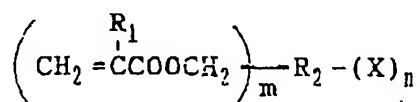
Examples of the inorganic acid that can be used in the present invention include nitric acid, phosphoric acid, hydrochloric acid and sulfuric acid. Among them, nitric acid and phosphoric acid can be preferably used. As the organic acid, there can be used monocarboxylic acid, dicarboxylic acid, tricarboxylic acid or tetracarboxylic acid. Examples of the monocarboxylic acid include formic acid, lactic acid, pyruvic acid, glycolic acid, chloroacetic acid, dichloroacetic acid, trichloroacetic acid, cyanoacetic acid and the like. Examples of the dicarboxylic acid include tartaric acid, succinic acid, glutaric acid, maleic acid, fumaric acid, malonic acid, citraconic acid, (o, m, p) phthalic acids and the like. Examples of the tricarboxylic acid include citric acid, tricarballic acid, 1,3,5-pentanetricarboxylic acid, trimellitic acid and the like. As desired, furthermore, a plurality of acids may be selected from the above-mentioned inorganic acids or the organic acids, and may be used being mixed together.

Among the above-mentioned acids, it is desired to use an organocarboxylic acid having an acid dissociation constant of not larger than 3 from the standpoint of adhesion to teeth and stimulation to dental pulp.

According to the first embodiment, the above-mentioned acid is blended in an amount of from 10 to 200 mmol and, preferably, from 15 to 150 mmol with respect to the total amount of 100 g of an acid group-containing (meth)acrylate monomer, an organosulfonate and/or an organosulfinate, a water-soluble organic solvent and the water. According to the second embodiment, the above-mentioned acid is blended in an amount of from 10 to 200 mmol and, preferably, from 15 to 150 mmol with respect to the total amount of 100 g of an acid group-containing (meth)acrylate monomer, an organosulfonate and/or an organosulfinate, a water-soluble organic solvent, the water and a hydroxy- or a dihydroxy(meth)acrylate monomer.

When the blending amount is larger than the above-mentioned range, smear plugs are completely removed. When the blending amount is smaller than the above-mentioned range, on the other hand, the enamel is not decalcified sufficiently. Among the aforementioned acids that are usually used in the form of an aqueous solution, the water in the aqueous solution is calculated as one of the components of the present invention as will be described later.

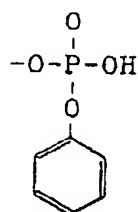
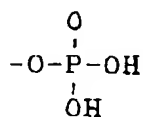
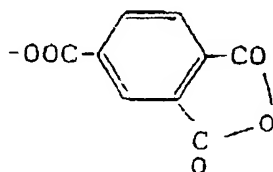
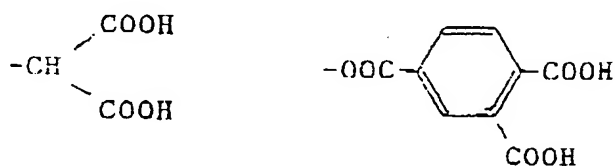
As the acid group-containing (meth)acrylate monomer of the present invention, there can be used any known compound provided it has a carboxyl group or an anhydride thereof, or an acid group such as phosphoric acid group in the molecules thereof. A representative example of the acid group-containing (meth)acrylate monomer is expressed by the following general formula,



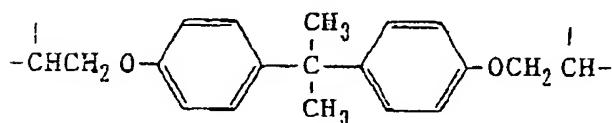
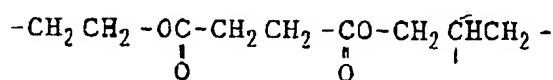
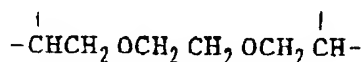
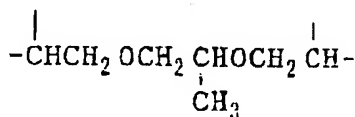
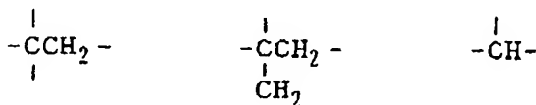
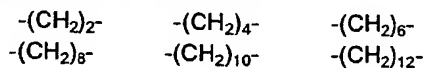
$$m = 1 - 4 \quad n = 1 \text{ or } 2$$

wherein R₁ is a hydrogen atom or a methyl group, R₂ is an organic residue having a valency of 2 to 6 and 1 to 20 carbon atoms, which may further have ether group and/or ester group, and X is a group containing carboxyl group, anhydrous carboxyl group, phosphoric acid group or phosphoric ester group.

In the above general formula, X is a group containing carboxyl group, anhydrous carboxyl group, phosphoric acid group or phosphoric ester group, and though there is no particular limitation on the structure thereof, its preferred examples are as described below.

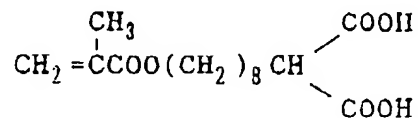


In the above-mentioned general formula, through there is no particular limitation on the structure, the organic residue R_2 has a valency of 2 to 6 and 1 to 20 carbon atoms and further has known ether group and/or ester group. Its concrete examples are as described below.

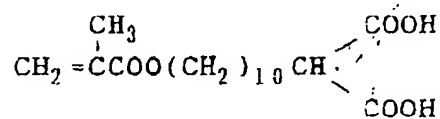


Preferred examples of the acid group-containing (meth)acrylate monomer expressed by the above-mentioned general formula are described below.

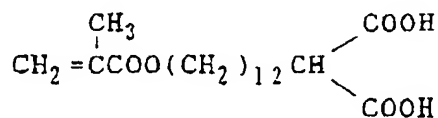
5



10

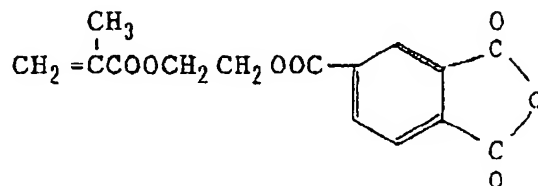


15

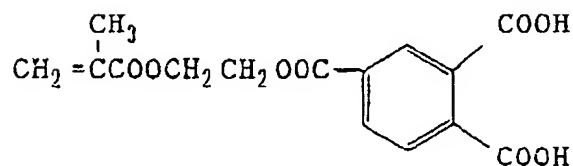


20

25

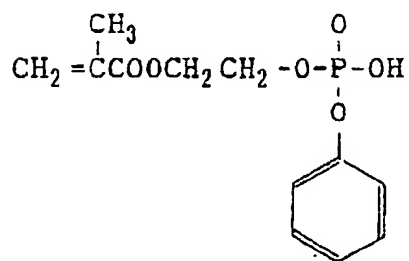


30



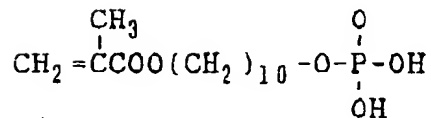
35

40



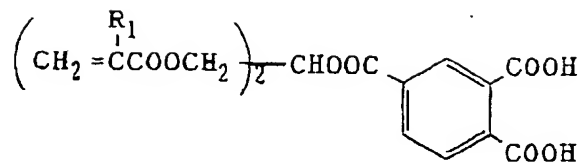
45

50

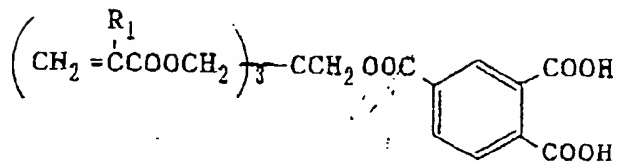


55

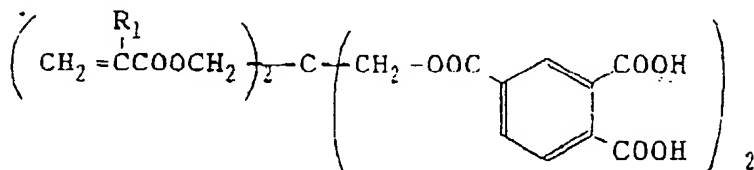
5



10

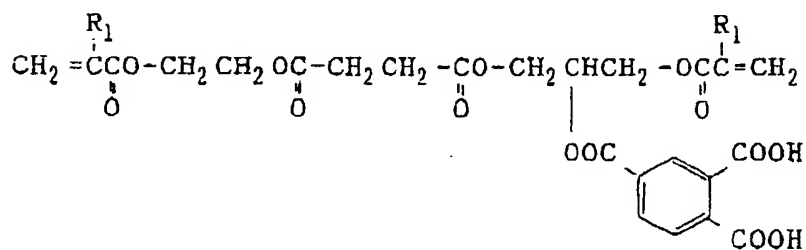


15



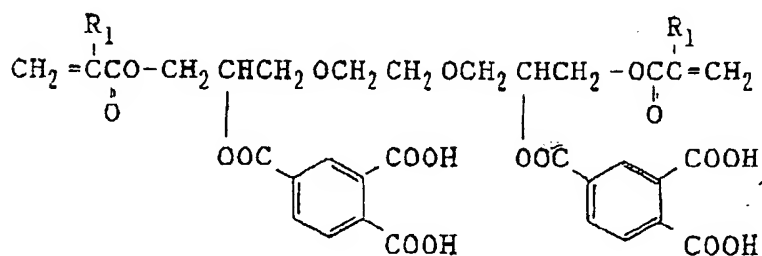
20

25



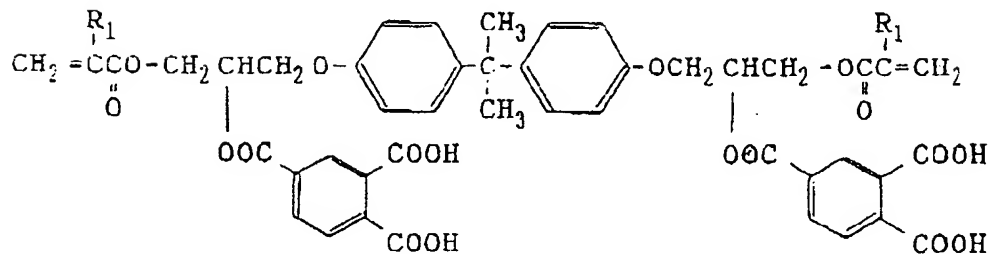
30

35



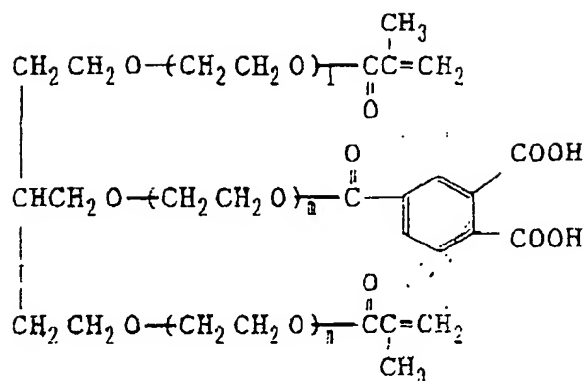
40

45

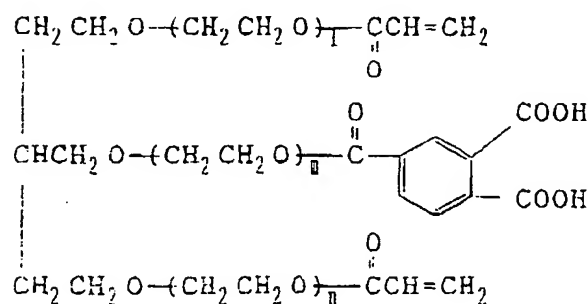


50

55



$$l + m + n = 3 - 5$$



$$l + m + n = 3 - 5$$

wherein R_1 is a hydrogen atom or a methyl group.

From the standpoint of adhesion to teeth, those having a carboxyl group or an anhydrous carboxyl group are particularly preferably used among the acid group-containing (meth)acrylate monomers that are concretely described above.

According to the first embodiment, the acid group-containing (meth)acrylate monomer is blended in an amount of from 1 to 30 parts by weight and, preferably, from 2 to 20 parts by weight with respect to the total amount of 100 parts by weight of the acid group-containing (meth)acrylate monomer, organosulfonate and/or organosulfinate, water-soluble organic solvent and water. According to the second embodiment, the acid group-containing (meth)acrylate monomer is blended in an amount of from 1 to 30 parts by weight and, preferably, from 2 to 20 parts by weight with respect to the total amount of 100 parts by weight of the acid group-containing (meth)acrylate monomer, organosulfonate and/or organosulfinate, water-soluble organic solvent, water and hydroxy- or dihydroxy(meth)acrylate monomer.

According to the first embodiment, addition of a polymerizable (meth)acrylate monomer other than the above-mentioned acid group-containing (meth)acrylate monomer should be avoided as it may deteriorate adhesion to the tooth. However, the hydroxy- or dihydroxy (meth)acrylate monomer helps increase the adhesion to both dentin and enamel when it is used in combination with the acid group-containing (meth)acrylate monomer.

Examples of the polymerizable (meth)acrylate monomer that should not be used include the following monomers; i.e., monofunctional monomers such as methyl methacrylate, ethyl methacrylate, tetrahydrofurfuryl methacrylate and acrylates thereof; aromatic bifunctional monomers such as

- 2,2-bis(4-methacryloyloxyethoxyphenyl) propane,
- 2,2-bis(4-methacryloyloxydiethoxyphenyl) propane,
- 2,2-bis(4-methacryloyloxytetraethoxyphenyl) propane,
- 2,2-bis(4-methacryloyloxyoctaethoxyphenyl) propane,
- 2,2-bis(4-methacryloyloxydipropoxyphenyl) propane,
- 2(4-methacryloyloxyethoxyphenyl)-2(4-methacryloyloxydiethoxyphenyl) propane,
- 2(4-methacryloyloxydiethoxyphenyl)-2(4-methacryloyloxytriethoxyphenyl) propane,
- 2(4-methacryloyloxydipropoxyphenyl)-2(4-methacryloyloxytriethoxyphenyl) propane,
- 2,2-bis(4-methacryloyloxydipropoxyphenyl) propane,

2,2-bis(4-methacryloyloxyisopropoxyphenyl) propane and acrylates thereof; aliphatic bifunctional monomers such as ethylene glycol dimethacrylate, diethylene glycol dimethacrylate, triethylene glycol dimethacrylate, butylene glycol dimethacrylate, neopentyl glycol dimethacrylate, propylene glycol dimethacrylate, 1,3-butanediol dimethacrylate, 1,4-butanediol dimethacrylate, 1,6-hexanediol dimethacrylate and acrylates thereof; trifunctional monomers such as trimethylolpropane trimethacrylate, trimethylolethane trimethacrylate, trimethylolpropane trimethacrylate and acrylates thereof; and tetrafunctional monomers such as pentaerythritol tetramethacrylate, pentaerythritol tetraacrylate and the like.

As the organosulfonate and/or organosulfinate that is used in the present invention, any known salts of organosulfonic acid or organosulfonic acid can be used without any particular limitation.

Examples of the organosulfonic acid that forms the organosulfonate include alkylsulfonic acids such as methanesulfonic acid, ethanesulfonic acid, and n-hexanesulfonic acid; aromatic sulfonic acids such as benzenesulfonic acid, o-toluenesulfonic acid, p-toluenesulfonic acid, ethylbenzenesulfonic acid, 4-aminobenzenesulfonic acid, 2-amino-5-methylbenzene-1-sulfonic acid, p-phenylsulfonic acid, decylbenzenesulfonic acid, dodecylbenzenesulfonic acid, and chlorobenzenesulfonic acid; and vinylsulfonic acids such as methallylsulfonic acid and p-methacryloxysulfonic acid. Among these organosulfonic acids, an aromatic sulfonic acid is desirably used from the standpoint of adhesion strength to the dentin.

Examples of the organosulfonic acid that forms the organosulfinate include alkylsulfonic acids such as methanesulfonic acid, ethanesulfonic acid and n-hexanesulfonic acid; and aromatic sulfonic acids such as benzenesulfonic acid, o-toluenesulfonic acid, p-toluenesulfonic acid, ethylbenzenesulfonic acid, decylbenzenesulfonic acid, dodecylbenzenesulfonic acid and chlorobenzenesulfonic acid. Among these organosulfonic acids, an aromatic sulfonic acid is desirably used from the standpoint of adhesive strength to teeth.

Examples of the cation that forms a salt with the above-mentioned organosulfonic acid or organosulfonic acid include alkali metals such as lithium, sodium and potassium; alkaline earth metals such as magnesium, calcium, strontium and barium; ammonium compounds such as ammonium, tetramethyl ammonium, tetraethyl ammonium, tetrapropyl ammonium and trimethylbenzyl ammonium; and amines such as methylamine, ethylamine, propylamine, butylamine, aniline, toluidine, phenylenediamine, piperidine, N-methylaniline, N-ethylaniline, diphenylamine, N-methyltoluidine, trimethylamine, triethylamine, N,N-dimethylaniline, pyridine, N,N-diethylaniline, N,N-dimethyltoluidine and the like.

The most preferred examples of the organosulfonate and/or organosulfinate include sodium p-toluene sulfonate, sodium benzene sulfonate, sodium dodecylbenzene sulfonate, sodium p-toluene sulfinate, lithium p-toluene sulfinate, sodium benzene sulfinate and lithium benzene sulfinate.

According to the first embodiment, the organosulfonate and/or organosulfinate is added in an amount of from 1 to 20 parts by weight with respect to the total amount of 100 parts by weight of the acid group-containing (meth)acrylate monomer, organosulfonate and/or organosulfinate, water-soluble organic solvent and water.

According to the second embodiment, the organosulfonate and/or organosulfinate is added in an amount of from 1 to 20 parts by weight with respect to the total amount of 100 parts by weight of the acid group-containing (meth)acrylate monomer, organosulfonate and/or organosulfinate, water-soluble organic solvent, water and hydroxy- or dihydroxy(meth)acrylate monomer.

In the present invention, the organosulfonate and the organosulfinate contribute to increasing the adhesive strength to teeth. Though the mechanism of action is not yet clear, it is presumed that they contribute to enhancing polymerization of the pre-treatment agent and of the adhesive at the interface of teeth.

According to the present invention, the water-soluble organic solvent is necessary for homogeneously dissolving other components. Its concrete examples include alcohols and ethers such as methanol, ethanol, propanol, butanol, ethylene glycol, propanediol, butanediol, pentanediol, butenediol, glycerin, trimethylolpropane, hexanetriol, allyl alcohol, diethylene glycol, diethylene glycol monomethyl ether, diethylene glycol monoethyl ether, triethylene glycol, triethylene glycol monomethyl ether, tetraethylene glycol, propylene glycol, dipropylene glycol, tripropylene glycol, 2-methoxyethanol, 2-ethoxyethanol, 2-(methoxyethoxy) ethanol, 2-isopropoxyethanol, 2-butoxyethanol, 1-methoxy-2-propanol, 1-ethoxy-2-propanol, dipropylene glycol, dipropylene glycol monomethyl ether, tripropylene glycol monomethyl ether, glycerine ether and the like, as well as ketones such as acetone, methyl ethyl ketone and the like.

Among them, it is desired to use those that are little harmful to the living body, such as ethanol, propanol, ethylene glycol, propanediol, butanediol, pentanediol, glycerine, trimethylolpropane, hexanetriol, allyl alcohol, diethylene glycol, diethylene glycol monomethyl ether, diethylene glycol monoethyl ether, triethylene glycol, triethylene glycol monomethyl ether, tetraethylene glycol, propylene glycol, dipropylene glycol, tripropylene glycol, dipropylene glycol, dipropylene glycol monomethyl ether, tripropylene glycol monomethyl ether, glycerine ether, acetone and the like. Most desirably, use is made of alcohols such as ethanol, propanol, ethylene glycol, propanediol and the like.

As required, two or more water-soluble solvents may be used being mixed together. When the above-

mentioned alcohols are to be used being mixed together with other water-soluble organic solvent, however, it is desired that the alcohols are added in an amount of not smaller than 30 parts by weight and, preferably, not smaller than 50 parts by weight with respect to the whole amount of the water-soluble organic solvent from the standpoint of forming a uniform film of the acid group-containing (meth)acrylate monomer and increasing the adhesive strength to teeth as will be described later.

According to the first embodiment, the water-soluble organic solvent is added in an amount of from 10 to 90 parts by weight with respect to the total amount of 100 parts by weight of the acid group-containing (meth)acrylate monomer, organosulfonate and/or organosulfinate, water-soluble organic solvent and water. According to the second embodiment, the water-soluble organic solvent is added in an amount of from 10 to 90 parts by weight with respect to the total amount of 100 parts by weight of the acid group-containing (meth)acrylate monomer, organosulfonate and/or organosulfinate, water-soluble organic solvent, water and hydroxy or dihydroxy (meth)acrylate.

According to the present invention, the water is necessary for decalcifying teeth. It is desired that the water does not substantially contain impurities that are detrimental to preservation stability, biocompatibility and adhesive property. Preferred examples include deionized water and distilled water.

According to the first embodiment, the water is added in an amount of from 5 to 80 parts by weight with respect to the total amount of 100 parts by weight of the acid group-containing (meth)acrylate monomer, organosulfonate and/or organosulfinate, water-soluble organic solvent and water. According to the second embodiment, the water is added in an amount of from 5 to 80 parts by weight with respect to the total amount of 100 parts by weight of the acid group-containing (meth)acrylate monomer, organosulfonate and/or organosulfinate, water-soluble organic solvent, water and hydroxy or dihydroxy (meth)acrylate.

The hydroxy or dihydroxyalkyl (meth)acrylate monomer used in the second embodiment helps further increase of adhesiveness to the tooth when it is used together with an acid group-containing (meth)acrylate monomer. Examples of this monomer include hydroxyethyl (meth)acrylate, hydroxypropyl (meth)acrylate, glyceryl mono(meth)acrylate, glyceryl di(meth)acrylate and the like. Preferably, however, there is used a monoester of a polyhydric alcohol with not more than 3 carbon atoms and a (meth)acrylic acid.

The hydroxy or dihydroxy(meth)acrylate monomer is added in an amount of from 1 to 40 parts by weight and, preferably, from 3 to 30 parts by weight with respect to the total amount of 100 parts by weight of the acid group-containing (meth)acrylate monomer, organosulfonate and/or organosulfinate, water-soluble organic solvent, water and hydroxy or dihydroxy(meth)acrylate monomer.

The composition of the present invention can be blended with a water-insoluble organic solvent and a viscosity-increasing agent in such small amounts as will not impair properties of the composition. Examples of the water-insoluble organic solvent will be hexane, heptane, octane, toluene, dichloromethane, chloroform, carbon tetrachloride, dichloroethane, trichloroethane, methyl ethyl ketone, pantanone, hexanone, ethyl formate, propyl formate, butyl formate, ethyl acetate, propyl acetate and butyl acetate. Examples of the viscosity-increasing agent include high molecular compounds such as polyvinyl pyrrolidone, carboxymethyl cellulose, polyvinyl alcohol and the like, as well as highly dispersing silica. Moreover, edible coloring matters may be blended as coloring materials.

There is no particular limitation on a process for preparing the composition of the present invention. The aforementioned acid, acid group-containing (meth)acrylate monomer, organosulfonate, organosulfinate, water and hydroxy- or dihydroxy(meth)acrylate monomer can be weighed at predetermined ratios, introduced into a container, and are stirred and mixed together until they are homogenized.

The dental composition of the present invention is used as a pre-treatment agent in the art of restoring a tooth by applying the pre-treatment agent to the tooth surfaces, washing the tooth with the water, drying the tooth, applying an adhesive to the tooth, curing the adhesive, packing a filling material, and curing the filling material. In order to obtain a favorable adhesive strength in this case, it has been confirmed that a film of an acid group-containing (meth)acrylate monomer should have been uniformly formed on the surface of the tooth after the pre-treatment agent is washed with the water. If the mechanism of adhesion is so postulated that a layer that contributes to adhesion is formed through diffusion of the applied adhesive component into the film of the acid group-containing (meth)acrylate monomer, then it can be presumed that formation of a uniform film is a prerequisite for forming the adhesive layer.

The manner of packaging the composition of the present invention can be suitably determined provided it does not impair the preservation stability. For instance, a solution of an organosulfonate and/or an organosulfinate and water, and another solution of an acid having pKa of not larger than 4, an acid group-containing (meth)acrylate monomer and a water-soluble organic solvent, are separately packaged, and are mixed together when they are to be used.

In order to use the composition of the present invention, however, all of the components must be mixed and treated simultaneously. For instance, a sufficiently large adhesion strength to the tooth is not obtained

even when the tooth surface is decalcified with a solution of an acid having pKa of not larger than 4, an acid group-containing (meth)acrylate monomer and a water-soluble organic solvent, and is washed with the water, dried and then a solution of an organosulfonate and/or an organosulfinate and water is applied thereto. Though the reason is not clear, it is considered that the acid group-containing (meth)acrylate monomer that is present in the step of decalcification the tooth infiltrates into the surface of the tooth.

For adhesion of the filling material to the tooth with an adhesive, pre-treating the surface of the tooth using the composition of the present invention makes it possible to process enamel and dentin simultaneously and besides permitting them to be highly strongly adhered together. Furthermore, smear plugs that are formed during cavity preparation and fill dentinal tubules are not excessively removed, and external stimulation is little probable to arrive at the dental pulp, which is a safer adhesion to the living body.

EXAMPLES

The composition of the present invention will now be concretely described by way of Examples to which only, however, the invention is in no way limited. Here, properties of the materials mentioned in the specification and Examples are measured as described below.

(1) Adhesive strength to the enamel and dentin.

A camphorquinone and an ethyl p-dimethylaminobenzoate ester were dissolved each in an amount of 0.2 g in 6 g of a bis-GMA, 21 g of a triethylene glycol dimethacrylate, 8 g of a hydroxyethyl methacrylate and 15 g of an 11-methacryloyloxy-1,1-undecanedicarboxylic acid to prepare a homogeneous solution which was used as an adhesive.

A bovine tooth was extracted within 24 hours after slaughtered, and enamel or dentin surface was ground using a #800 emery paper to be in parallel with the facial surface while pouring the water. The compressed air was blown to the surface of the dentin for about 10 seconds to dry it, and the dentin was treated with the pre-treatment agent which was the composition of the present invention for 20 seconds. Then, the treated surface was washed with the water, dried, and a double-sided tape having a hole 4 mm in diameter was adhered to the surface. Then, a paraffin with a hole which is 1.5 mm thick and 6 mm in diameter was fitted onto the above-mentioned hole in concentric therewith to imitate dental cavity. Then, the adhesive was applied thereto and was cured with light irradiation for 10 seconds by using a visible light irradiator (Witelite, produced by Takara Belmont Co.). Then, a dental composite resin (Palfique Estelite produced by Tokuyama Soda Co.) was applied thereon and was irradiated with light for 30 seconds using the visible light irradiator to prepare an adhesion test piece.

After immersed in the water at 37 °C for 24 hours, adhesive strength of the test piece was measured by using a tension tester (Autograph, produced by Shimazu Mfg. Co.) at a crosshead speed of 10 mm/min.

Adhesion strength to enamel is greatly affected by the degree of decalcification, and the adhesion strength increases with an increase in the degree of decalcification. In order to prevent the formation of a gap between the filling material and the surface of dentin, the adhesion strength to the enamel must be about 15 MPa. There does not exist any relationship between the degree of decalcification of dentin and the adhesive strength.

(2) Degree of decalcification of dentin.

A front tooth was removed from a cow within 24 hours after it was slaughtered, and the dentin surface was ground and exposed using a #800 emery paper to be in parallel with the facial surface while pouring the water. The compressed air was blown to the surface of the dentin for about 10 seconds to dry it, and the dentin was treated with the pre-treatment agent which was the composition of the present invention and was left to stand for a predetermined period of time. After the surface applied with the pre-treatment agent was washed with the water, 20 dentinal tubules appearing on a screen were observed by using a scanning electron microscope (produced by Nihon Denshi Co.) in order to evaluate the degree of decalcification in terms of a ratio of the opening areas of the tubules. That is, the degree of decalcification was evaluated in six stages in which 0 was the case where the decalcification progressed up to peritubular dentin, 1 was the case where the opening degree of tubules 100 to 80%, 2 was the case where the opening degree of fine tubes was 80 to 60%, 3 was the case where the opening degree of tubules was 60 to 40%, 4 was the case where the opening degree of tubules was 40 to 20%, and 5 was the case where the opening degree of tubules was 20 to 0%. Usually, it is judged that dentin is favorably decalcified when the opening degree is from 40 to 0%, or from 4 to 5 in the evaluation of six stages.

Described below are abbreviations representing compounds appearing in Tables in Examples and in Com-

parative Examples.

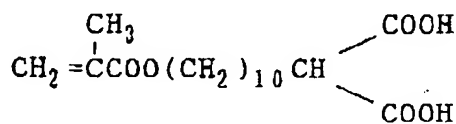
PTSI-Na: sodium p-toluenesulfonic acid
 PTSO-Na: sodium p-toluenesulfonic acid
 PTSI-Li: lithium p-toluenesulfonic acid
 DBSO-Na: sodium dodecylbenzenesulfonic acid
 BSI-Na: sodium benzenesulfonic acid
 BSO-Na: sodium benzenesulfonic acid
 BSI-Li: lithium benzenesulfonic acid
 DGME: diethylene glycol monoethyl ether
 HEMA: hydroxyethyl methacrylate
 HPMA: hydroxypropyl methacrylate
 GMMA: glyceryl monomethacrylate
 TEGDMA: triethylene glycol dimethacrylate
 c-HMA: cyclohexyl methacrylate

(Example 1)

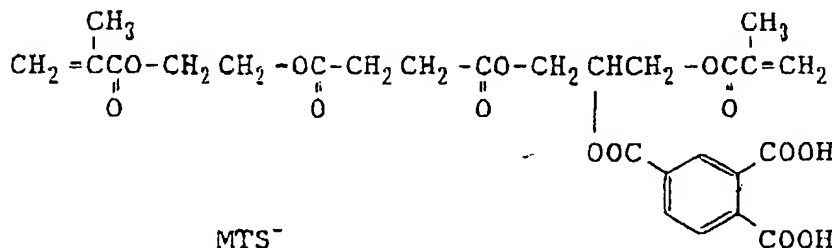
1.2 Grams of maleic acid, 1.0 g of a sodium p-toluenesulfinate, 3.0 g of ethanol and 6.0 g of distilled water were mixed together to obtain a homogeneous solution thereof. 1.0 Grams of an 11-methacryloyloxy-1,1-un-decanedicarboxylic acid (hereinafter referred to as MAC-10) and 9.0 g of ethanol were mixed together to obtain another homogeneous solution thereof. The two solutions were mixed together at a weight ratio of 1:1 to obtain a pre-treatment agent which was used to measure the adhesion strength to the enamel and dentin and to measure the degree of deliming the dentin. The results were shown in Table 1. In Tables 1 and 2, the amounts of acids are in millimols per a total of 100 g of the acid group-containing (meth)acrylate monomer, organosulfonate and/or organosulfinate, water-soluble organic solvent and water.

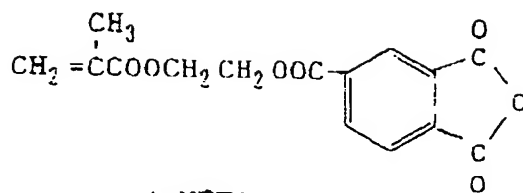
(Examples 2 to 10)

Pre-treatment agents having compositions shown in Table 1 were prepared in accordance with the method of Example 1 in order to measure the adhesive strength to the enamel, adhesive strength to dentin and the degree of decalcification of dentin. The results were as shown in Table 2. Described below are the structures and abbreviations of the acid group-containing (meth)acrylate monomers that were used.



MAC-10





5

10

15

20

25

30

35

40

45

50

55

Table 1

| Example | Acid | pKa (mmol) | Acid group- containing (meth)acrylate monomer (wt%) | Organosulfonate/ organosulfinate (wt%) | Water-soluble organic solvent (wt%) | Water (%) | Hydroxy, dihydroxy (meth)- acrylate, monomer (wt%) |
|------------|-----------------|------------|--------------------------------------------------------------|----------------------------------------------|-------------------------------------------|--------------|-------------------------------------------------------------------|
| Example 1 | maleic acid | 1.92 | 52 MAC-10 | 5 PTSI-Na | 60 ethanol | 30 | — |
| Example 2 | maleic acid | 1.92 | 52 MTS | 5 PTSO-Na | 15 acetone 10 ethanol | 65 | — |
| Example 3 | nitric acid | <4 | 19 MAC-10 | 18 PTSI-Li | 2 ethanol | 50 | — |
| Example 4 | phosphoric acid | 2.15 | 110 MAC-10 | 3 OBSO-Na | 12 isopropanol | 55 | — |
| Example 5 | tartaric acid | 3.04 | 70 4-META | 12 BSI-Na | 5 ethanol 55 chloroform | 13 | — |
| Example 6 | citric acid | 3.16 | 80 MAC-10 | 8 BSO-Na | 15 isopropanol | 37 | — |
| Example 7 | maleic acid | 1.92 | 60 MAC-10 | 5 PTSI-Na | 30 ethanol 30 DGME | 30 | — |
| Example 8 | maleic acid | 1.92 | 52 MAC-10 | 5 PTSI-Na | 20 ethanol | 50 | HEMA 20 |
| Example 9 | citric acid | 3.16 | 86 MTS | 10 BSO-Na | 25 ethanol | 40 | HPMA 10 |
| Example 10 | nitric acid | <4 | 20 MAC-10 | 15 BSI-Li | 20 ethanol | 15 | GMMA 40 |

Table 2

| | Deg. of decalcification of dentin | Adhesive strength to dentin (MPa) | Adhesive strength to enamel (MPa) |
|------------|-----------------------------------|-----------------------------------|-----------------------------------|
| Example 1 | 5 | 16.1 | 17.1 |
| Example 2 | 5 | 15.3 | 15.2 |
| Example 3 | 4 | 16.3 | 16.0 |
| Example 4 | 5 | 14.5 | 17.4 |
| Example 5 | 5 | 14.0 | 14.9 |
| Example 6 | 5 | 14.7 | 15.2 |
| Example 7 | 4 | 16.1 | 15.9 |
| Example 8 | 5 | 19.3 | 18.2 |
| Example 9 | 5 | 18.1 | 17.2 |
| Example 10 | 4 | 18.5 | 17.7 |

Examples 1, 2 and 5 represent the results with different acid group-containing (meth)acrylate monomers, and Examples 1, 3, 4, 5 and 6 represent the results with different acids. Examples 3 and 4 represent ranges of testing the amounts of acids and acid group-containing (meth)acrylate monomers, Examples 3, 6 and 9 represent ranges of testing the amounts of the organosulfonate or the organosulfinate, and Examples 2 and 5 represent ranges of testing the amounts of the water-soluble organic solvent and the water. The pre-treatment agent of Example 5 contains a small amount of chloroform which is a water-insoluble solvent in addition to the water-soluble solvent. In all other examples, water-soluble organic solvents only are used as the organic solvents. Examples 2 and 7 are the cases where water-soluble organic solvents are mixed, and Examples 8, 9 and 10 are cases where a hydroxymethacrylate monomer is added. The above-mentioned Examples all exhibited favorable results concerning the degree of decalcification of dentin, adhesive strength to dentin and adhesive strength to enamel.

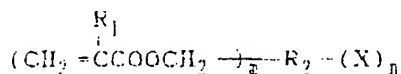
(Comparative Examples 1 to 10)

Pre-treatment agents having compositions shown in Table 3 were prepared according to the same method as that of Example 1 and were evaluated. Table 3 shows the compositions of the pre-treatment agents and Table 4 shows the results.

Table 3

| Acid | | pKa (mmol) | Acid group- containing (meth)acrylate monomer (wt%) | Organosulfonate/ organosulfinate (wt%) | Water-soluble organic solvent (wt%) | Water (%) | Meth-, acrylate monomer (wt%) | | | |
|---------------------|----------------|------------|--------------------------------------------------------------|----------------------------------------------|-------------------------------------------|--------------|----------------------------------------|----|--------|----|
| | | | | | | | | | | |
| Comp. Example 1 | maleic acid | 1.92 | 200 | MAC-10 | 5 | PTSI-Na | 60 | 30 | — | — |
| Comp. Example 2 | maleic acid | 1.92 | 8 | MAC-10 | 5 | PTSI-Na | 60 | 30 | — | — |
| Comp. Example 3 | maleic acid | 1.92 | 52 | MAC-10 | 0 | PTSI-Na | 60 | 35 | — | — |
| Comp. Example 4 | maleic acid | 1.92 | 52 | MAC-10 | 33 | PTSI-Na | 42 | 20 | — | — |
| Comp. Example 5 | maleic acid | 1.92 | 52 | MAC-10 | 5 | PTSI-Na | 90 | 0 | — | — |
| Comp. Example 6 | maleic acid | 1.92 | 52 | MAC-10 | 5 | PTSI-Na | 0 | 90 | — | — |
| Comp. Example 7 | maleic acid | 1.92 | 52 | MAC-10 | 5 | — | 60 | 35 | — | — |
| Comp. Example 8 | acetic acid | 4.76 | 52 | MAC-10 | 5 | PTSI-Na | 60 | 30 | — | — |
| Comp. Example 9 | maleic acid | 1.92 | 52 | MAC-10 | 5 | PTSI-Na | 45 | 30 | TEGDMA | 15 |
| Comp. Example 10 | maleic acid | 1.92 | 52 | MAC-10 | 5 | PTSI-Na | 50 | 30 | c-HMA | 10 |

(B) is of the formula,



wherein R_1 is a hydrogen atom or a methyl group, R_2 is an organic residue having a valency of 2 to 6 and - containing 1 to 20 carbon atoms optionally further comprising one or more ether and/or ester groups, X is a carboxyl group, carboxylic anhydride group, phosphoric acid group or phosphoric ester group, m is from 1 to 4, and n is 1 or 2

5. A composition according to claim 4 wherein R_2 is a hydrocarbyl group containing from 1 to 20 carbon atoms, optionally further comprising one or more ether and/or ester groups.
6. A composition according to any one of the preceding claims wherein the organosulfinate or organosulfonate (C) is an alkali metal salt of an aromatic sulfinate or sulfonate.
7. A composition according to claim 6 wherein (C) is an alkali metal salt of an aromatic sulfinate.
8. A composition according to any one of the preceding claims wherein the water-soluble organic solvent (D) is an alcohol.
9. A composition according to any of claims 2 to 8 wherein the hydroxy- or dihydroxyalkyl(meth)acrylate monomer is a monoester of a polyhydric alcohol having not more than 3 carbon atoms and a (meth)acrylic acid.
10. A composition according to any one of claims 1 or 3 to 8 which does not comprise a polymerizable (meth)acrylate monomer other than the acid group-containing (meth)acrylate monomer (B).
11. An agent suitable for pre-treating the surface of a tooth comprising a dental composition as claimed in any one of the preceding claims.



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 94 30 9772

| DOCUMENTS CONSIDERED TO BE RELEVANT | | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------|----------------------------------------------|
| Category | Citation of document with indication, where appropriate, of relevant passages | Relevant to claim | CLASSIFICATION OF THE APPLICATION (Int.Cl.6) |
| Y | EP-A-0 305 083 (MINNESOTA MINING & MFG) 1 March 1989 * page 3, line 7 - page 5, line 40; claims * | 1-11 | A61K6/00 A61K6/083 |
| Y,P | --- PATENT ABSTRACTS OF JAPAN vol. 018 no. 542 (C-1261) ,17 October 1994 & JP-A-06 192030 (TOKUYAMA SODA CO LTD) 12 July 1994, * abstract * | 1-11 | |
| A,D | --- DATABASE WPI Section Ch, Week 8532 Derwent Publications Ltd., London, GB; Class A14, AN 85-194682 & JP-A-60 123 515 (MITSUI PETROCHEM IND KK) , 2 July 1985 * abstract * | | |
| A | --- EP-A-0 408 357 (KURARAY CO) 16 January 1991 * claims * | 6 | TECHNICAL FIELDS SEARCHED (Int.Cl.6) |
| A | --- EP-A-0 206 810 (TOKUYAMA SODA KK) 30 December 1986 ----- | | A61K |
| The present search report has been drawn up for all claims | | | |
| Place of search THE HAGUE | | Date of completion of the search 13 April 1995 | Examiner Cousins-Van Steen, G |
| CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document | | | |

EPO FORM 1503 01.92 (P04C01)